Remarks

Claims 1-4, 7, 8, 42, 43 and 58-77 are pending in this application. Applicants have amended claims 1-3 to further clarify the claim language. No new matter has been added.

Rejections Under 35 U.S.C. 112, First Paragraph

Enablement Rejection of Claims 1-3, 7, 42, 43, 58-63, 66-68, 70-73 and 75-76 Under 35 U.S.C. 112, First Paragraph

The Examiner rejected claims 1-3, 7, 42, 43, 58-63, 66-68, 70-73 and 75-76 under 35 U.S.C. 112, first paragraph as not enabled. Applicants have made amendments to the claims and respectfully request reconsideration of the claims as amended.

The Examiner stated that the specification, while being enabling for the recited peptides which bind to the HLA class I molecule of HLA Cw*07, does not reasonably provide enablement for the recited peptides which bind to any HLA class I molecule. In support of the rejection, the Examiner stated that "Engelwood [sic, Engelhard] discloses that the anchor amino acids within the peptide are important for binding specifically to each MHC Class I molecule. Since the specification does not disclose any HLA Class I molecule, other than the HLA Cw*07, that binds the peptides encompassed by the instant claims, it would require undue experimentation for one of skill to predict which HLA molecule, other than HLA Cw*07, would bind the peptides encompassed by the instant claims, without further guidance from the instant specification." Based on this, the Examiner concluded that in view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue "trials and errors" to practice the claimed invention.

Applicant respectfully notes that persons of ordinary skill in the art are familiar with methods to determine the binding of peptides to HLA molecules. Applicant has provided a description of such methods in the specification (see Example 1 for description of CTL lysis (chromium release) and CTL stimulation (TNF release) assays). In addition, the art is familiar

with HLA-peptide binding assays, which had been known for many years prior to the filing of the application. Therefore, given that Applicant has provided peptide sequences, it would require nothing more than routine experimentation utilizing standard, well-established peptide binding assays to determine if a HLA-C molecule binds to the claimed peptides.

Moreover, the person of skill in the art is familiar with the importance of anchor residues in the HLA class I binding characteristics of peptides. As such, the art is familiar with references such as Falk et al., *Proc. Natl. Acad. Sci. USA* 90:12005-12009, 1993 (copy enclosed), which shows that consensus binding motifs of HLA-Cw3, Cw4, Cw6 and Cw7 have a strong preference for leucine (L) at residue 9 and a weaker preference for arginine (R) at residue 2. The peptides derived from MAGE A12 (e.g., VRIGHLYIL) satisfy these binding preferences, particularly with the strong preference for Leu at position 9 anchoring the peptide binding.

Taken together, the foregoing indicates that undue experimentation would not be required of one of ordinary skill in the art to practice the claimed invention. Even assuming that the Examiner is correct regarding the unpredictability of the art (which Applicant cannot agree with given the disclosure of the sequences in the application), the ease with which one of ordinary skill in the art can determine the binding capabilities of a peptide strongly argue for enablement of the claimed invention.

Accordingly, Applicant respectfully requests that the rejection of claims 1-3, 7, 42, 43, 58-63, 66-68, 70-73 and 75-76 under 35 U.S.C. 112, first paragraph, be withdrawn.

Written Description Rejection of Claims 1-3, 7, 42-43, 58-63, 66-68, 70-73 and 75-76 Under 35 U.S.C. 112, First Paragraph

The Examiner rejected claims 1-3, 7, 42-43, 58-63, 66-68, 70-73 and 75-76 under 35 U.S.C. §112, first paragraph, as lacking an adequate written description. Applicants have made amendments to the claims to state that the specificity of binding is to HLA-C molecules, and accordingly respectfully request reconsideration of the claims as amended.

The Examiner stated that there is no description in the specification of the structural features required by the wide range of HLA class I molecules encompassed by the instant claims.

Applicant's amendment to the claims reduces the range of HLA molecules to HLA-C molecules. These molecules are a class of proteins that is known in the art. As noted above, the binding specificities of HLA-C molecules are known (Applicant notes that the Falk et al. reference is merely an example of the knowledge in the art regarding HLA-C motifs, not the full extent of that knowledge). Thus the person of skill in the art would understand from a reading of Applicant's specification that Applicant was in possession of the claimed peptides and that these peptides would bind to HLA-C molecules in addition to the specific example shown in the Examples.

Accordingly, Applicant respectfully requests that the rejection of claims 1-3, 7, 42-43, 58-63, 66-68, 70-73 and 75-76 under 35 U.S.C. §112, first paragraph, be withdrawn.

Enablement Rejection of Claims 4, 8, 64-65, 74 and 77 Under 35 U.S.C. 112, First Paragraph

The Examiner rejected claims 4, 8, 64-65, 74 and 77 under 35 U.S.C. 112 first paragraph, as not enabled. Specifically, the Examiner stated that the specification does not reasonably provide enablement for an isolated MAGE-A12 class I binding peptide which binds HLA Cw*07, wherein said peptide consists of any fragment of SEQ ID NO:2. Applicant respectfully traverses the rejection.

The Examiner stated that the specification does not disclose fragments of SEQ ID NO:2 which bind HLA Cw*07, other than the fragments consisting of SEQ ID NO:4, 5, or 6. Applicant respectfully disagrees. In Example 1 of the specification, Applicant disclosed that: "Cells transfected with fragments of 540 bp or more were capable of stimulating CTL 501D/19, whereas those transfected with shorter fragments were not. This indicated that the end of the sequence coding for the antigenic peptide was located between nucleotide 525 and 540 of the MAGE-A12 ORF." This is clearly demonstrated in Fig. 3, which shows that various truncated MAGE-A12 proteins were capable of binding to HLA-Cw7. This indicates that the presence of the HLA-Cw7 binding portion of MAGE-A12 is sufficient to confer on fragments of MAGE-A12 the ability to bind HLA-Cw7 and to stimulate CTL activity as shown in Fig. 3.

As is well known in the art, polypeptides that are longer than a HLA binding peptide will be processed to an appropriate size. Applicant stated in the Background of the Invention section of the specification that a T cell immune response "requires that T cells recognize and interact with complexes of cell surface molecules, referred to as human leukocyte antigens ("HLA"), or major histocompatibility complexes ("MHCs"), and peptides. The peptides are derived from larger molecules which are processed by the cells which also present the HLA/MHC molecule." (emphasis added). Appropriate processing of MAGE-A12 fragments is demonstrated in Fig. 3.

Therefore, Applicant has enabled one of ordinary skill in the art to make and use HLA-Cw7 binding fragments of MAGE-A12, as long as the fragment contains the HLA-Cw7 binding portion identified by Applicant. No undue experimentation or prediction of fragments is required because the disclosure in the specification clearly demonstrates (by a working example) that fragments of MAGE-A12 can be appropriately processed and presented by HLA-Cw7, and further because the person of skill in the art routinely generates protein fragments as are claimed in the instant application.

Accordingly, Applicant respectfully requests that the rejection of claims 4, 8, 64-65, 74 and 77 under 35 U.S.C. §112, first paragraph, be withdrawn.

Written Description Rejection of Claims 4, 8, 64-65, 74 and 77
Under 35 U.S.C. 112, First Paragraph

The Examiner also rejected claims 4, 8, 64-65, 74 and 77 under 35 U.S.C. §112, first paragraph, as lacking an adequate written description.

The Examiner stated that the specification does not disclose fragments of SEQ ID NO:2 which bind HLA-Cw*07, other than the fragments consisting of SEQ ID NO:4, 5, or 6. As noted above, this is incorrect. Regarding structural features required by fragments of SEQ ID NO:2 for binding HLA-Cw*07, Applicant notes that the specification discloses that SEQ ID NO:4, 5, or 6 contain the structural features required for binding.

Moreover, Applicant showed that the only other peptide predicted to bind HLA-Cw7 in the region of MAGE-A12 demonstrated to confer HLA-Cw7 binding (see Example 1),

EVVRIGHLY (SEQ ID NO:3), was not recognized by HLA-Cw7. Therefore, the required structural features were clearly delineated by Applicant in a manner that would indicate to one of ordinary skill in the art that Applicant was in possession of the invention.

Accordingly, Applicant respectfully requests that the rejection of claims 4, 8, 64-65, 74 and 77 under 35 U.S.C. §112, first paragraph, be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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